REMARKS

Claims 1-94 are pending in this application. Claims 1 and 27 have been amended to clarify the definition of variable R_{19}. Claims 20 and 31-34 have been amended to avoid use of the word "preferable" in the claims. New claims 89-93 recite certain subject matter previously identified as "preferable" in claims 20 and 31-34. New claim 94 recites a compound exemplified at page 108, Example 7Z. None of the amendments have narrowed the scope of any claims.

Applicants have also added an Abstract of appropriate length.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

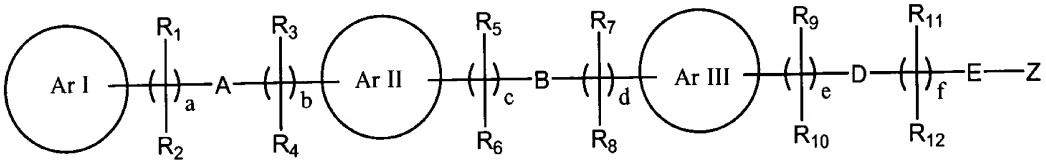
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____
Steven J. Scott
Reg. No. 43,911

Date: February 25, 2002

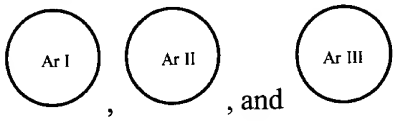
Appendix Detailing Amendments to Claims

1. (Amended) A compound of formula I



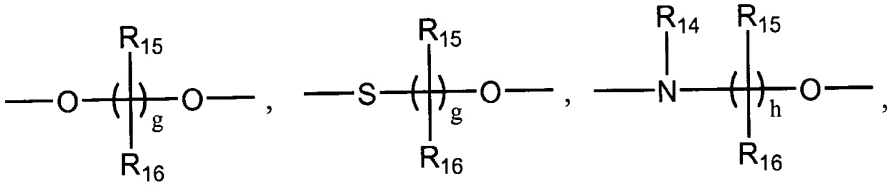
(I)

wherein:



, and are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkenyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl;

A is -O-, -S-, -SO-, -SO_2-, -NR_{13}-, -C(O)-, -$N(R_{14})C(O)$-, -$C(O)N(R_{15})$-, -$N(R_{14})C(O)N(R_{15})$-, -$C(R_{14})$=N-, a chemical bond,



B is –O-, -S-, -SO-, -SO_2-, -NR_{17}-, a chemical bond, ethynylene, -C(O)-, -$N(R_{18})C(O)$-, or –$C(O)NR_{18}$-;

D is –O-, -S-, -NR_{19}-, a chemical bond, ethynylene, -$N(R_{20})C(O)$-, -C(O)-, or –$C(O)N(R_{20})$-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R_1, R_3, R_5, R_7, R_9, and R_{11}, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R_2, R_4, R_6, R_8, R_{10} and R_{12}, are independently $-(CH_2)_q-X$;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acyl$HNSO_2$-, $-SR_{23}$, Y^1Y^2N- or Y^3Y^4NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C$-, $R_{21}OC$-, cyclo-imide, -CN, $R_{21}O_2SHNCO$-, $R_{21}O_2SHN$-, $(R_{21})_2NCO$-, $R_{21}O$- 2,4-thiazolidinedionyl, or tetrazolyl; and

[R_{19} and] R_{21} <u>is</u> [are independently] hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13}, R_{17}, R_{19} and R_{23} are independently $R_{22}OC$-, $R_{22}NHOC$-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14}, R_{15}, R_{16}, R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14}, and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group;or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

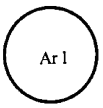
when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

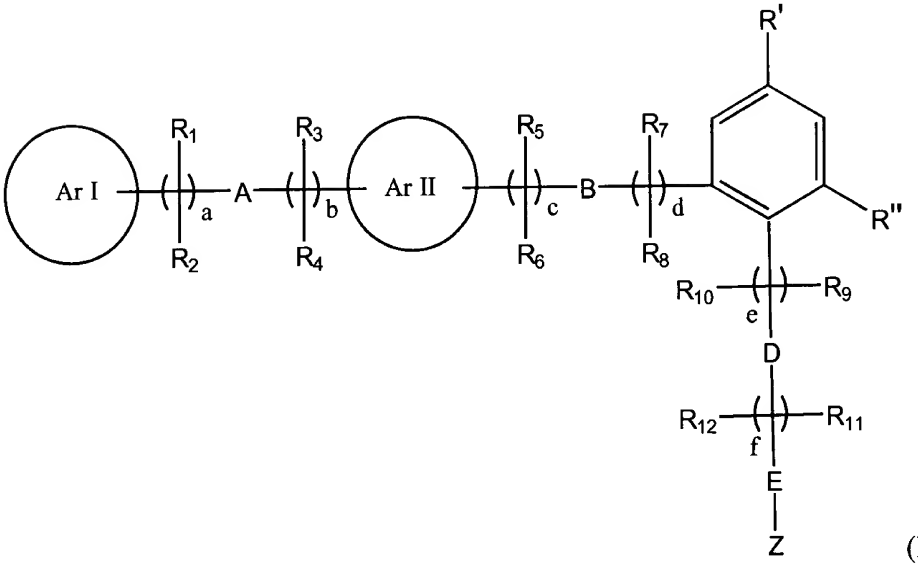
R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

20. (Amended) A compound according to claim 1 wherein 

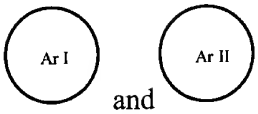
is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, *N*-alkyl-quinolin-4-onyl, quinazolin-4-onyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, indolinyl oxazolyl, thiazolyl, oxadiazolyl isoxazolyl, imidazolyl, pyrazol-yl, thiadiazolyl, triazolyl, pyridyl pyrimidinyl, pyrazinyl, pyridazinyl, phenyl, or napthalenyl group, wherein the substituent is a ring system substituent [as defined herein , more preferably a substituent selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, lower alkyl, branched alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy].

27. (Amended) A compound of formula (Ia)



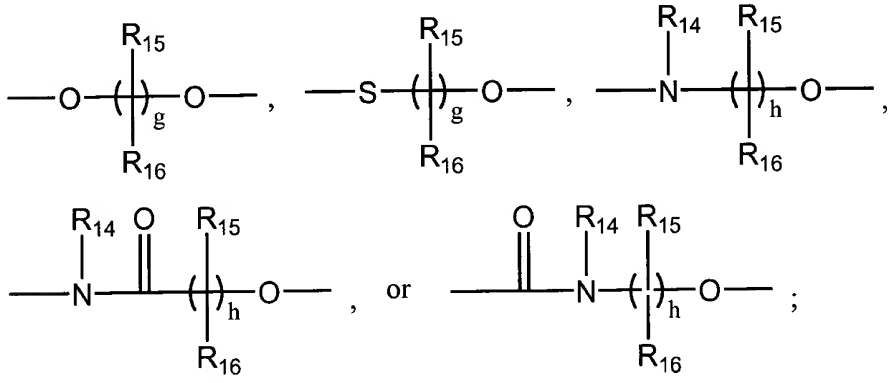
(Ia)

wherein:



and are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkenyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl;

A is -O-, -S-, -SO-, -SO_2-, -NR_{13}-, -C(O)-, -$N(R_{14})C(O)$-, -$C(O)N(R_{15})$-, -$N(R_{14})C(O)N(R_{15})$-, -$C(R_{14})$=N-, a chemical bond,



B is –O-, -S-, -SO-, -SO_2-, -NR_{17}-, a chemical bond, ethynylene, -C(O)-, -$N(R_{18})C(O)$-, or –$C(O)NR_{18}$-;

D is –O-, -S-, -NR_{19}-, a chemical bond, ethynylene, -$N(R_{20})C(O)$-, -C(O)-, or –$C(O)N(R_{20})$-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R_1, R_3, R_5, R_7, R_9, and R_{11}, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R_2, R_4, R_6, R_8, R_{10} and R_{12}, are independently $-(CH_2)_q-X$;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO$_2$-, -SR$_{23}$, Y^1Y^2N- or Y^3Y^4NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C$-, $R_{21}OC$-, cyclo-imide, -CN, $R_{21}O_2SHNCO$-, $R_{21}O_2SHN$-, $(R_{21})_2NCO$-, $R_{21}O$- 2,4-thiazolidinedionyl, or tetrazolyl;

R' and R" are ring system substituents;

[R_{19} and] R_{21} <u>is</u> [are independently] hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13}, R_{17}, R_{19} and R_{23} are independently $R_{22}OC$-, $R_{22}NHOC$-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14}, R_{15}, R_{16}, R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14}, and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group;or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

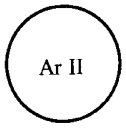
31. (Amended) A compound according to claim 27 wherein

a = 1 or 2;

A is -O-;

b = 0;

R_1, R_2, R_7 and R_8 are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, halo or benzyloxy;

R" is lower alkyl [, preferably methyl];

Z is $-CO_2H$.

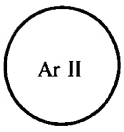
32. (Amended) A compound according to claim 27 wherein:

a = 1 or 2;

A is -O-;

b = 0;

R_1, R_2, R_5 and R_6 are independently hydrogen;



is optionally substituted phenyl;

c = 1;

B is -O-;

d = 0;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, halo or benzyloxy;

R" is lower alkyl [, preferably methyl];

Z is $-CO_2H$.

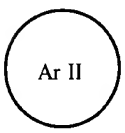
33. A compound according to claim 27 wherein:

a = 1 or 2;

A is -O-;

b = 0;

R_1, R_2, R_7, R_8, R_{11} and R_{12} are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 1;

D and E are a chemical bond;

R' is halo;

R" is lower alkyl [, preferably methyl];

Z is $-CO_2H$.

34. (Amended) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0-1;

B is -O-;

d = 0 or 1, wherein c+d = 1 or 2;

e = 0;

f = 0;

D and E are a chemical bond;

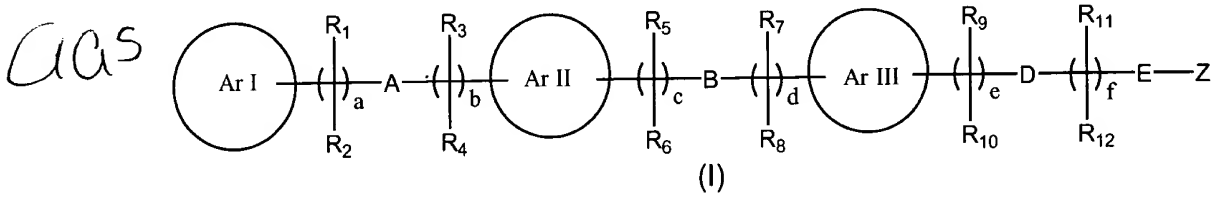
R' is hydrogen, aralkoxy, or halo;

R" is lower alkyl [, preferably methyl];

Z is $-CO_2H$.

Abstract

The use of triaryl acid derivatives of formula (I)



(I)

and their pharmaceutical compositions as PPAR ligand receptor binders. The PPAR ligand receptor binders of this invention are useful as agonists or antagonists of the PPAR receptor.